IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sun, et al.
Title:	METHODS AND COMPOSITIONS FOR THE DETECTION OF MUCOLIPIDOSIS IV MUTATIONS
Appl. No.:	10/754,446
Filing Date:	January 9, 2004
Examiner:	Kapushoc, Stephen Thomas
Art Unit:	1634
Confirmation Number:	7990

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below.

Marisol Moretto
(Printed Name)

(Signature)

August 10, 2006
(Date of Deposit)

DECLARATION OF WEIMAN SUN, PH.D UNDER 37 C.F.R §1.132

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

I, Weiman Sun, Ph.D. hereby declare as follows:

1. I attended the University of California, Davis where I received a Ph.D degree in Pharmacology and Toxicology in 1994.

2. I was a postdoctoral fellow at UCLA Intercampus Medical Genetics Training program for over 3 years. Then, I served as the director of the molecular genetics laboratory (The Genetics Center) and the manager of the molecular pathology lab (UC Irvine) before joining Quest Diagnostics as an associate scientific director and later the R&D manager of the Molecular Genetics Department. I am currently the Scientific Director of Molecular Genetics at Quest Diagnostics Nichols Institute, Assignee of the patent application.

3. In total, I have worked more than 12 years in the field of nucleic acid diagnostic assays. I am the author or co-author of more than 29 published scientific articles and

many abstracts in this field. A brief summary of my accomplishments and a recent copy of my Curriculum Vitae is attached as APPENDIX 1.

4. I am a co-inventor of the above identified patent application. I understand that the Examiner has rejected the claims as being obvious over a combination of prior art references. According to the Examiner, one of ordinary skill would have been motivated to take various features from these references and combine them to obtain the claimed invention and that there would have been a reasonable expectation of success in achieving the combination. The Examiner bases this conclusion on the belief that because the entire sequence of MCOLN1 is known, it would have required nothing more than ordinary skill to develop a MCOLN1 real time assay using any particular primer or probe sequence that can be derived from the MCOLN1 genome. In my opinion, this rationale is flawed. My own experience from 12 years of assay development and from others who have published in this field leads me to conclude that a successful nucleic acid based assay is very much dependent on the particular primers and probe sequences chosen and that there is no way to predict in advance whether particular sequences would be effective.

5. It is my experience that real time amplification assays such as the TaqMan assay are more complex than standard PCR assays because the primers and the probe in a TaqMan format must be able to function together at the same time since the probe must bind to amplified product as it is extended from the primers. The probe in standard PCR is applied after the PCR has been completed and amplicons generated. Because of the more stringent working requirements, primers pairs and probes that might work acceptably in standard PCR are more likely to fail or perform poorly in the TaqMan format. I conclude from this that there would not have been a reasonable expectation of success for combining the probes of Edelmann et al. from standard PCR assays, for use in a TaqMan style PCR assay such as described in Doll et al. as asserted by the Examiner.

6. Unlike mutation analysis methods that analyze amplification products from conventional PCR reactions, our amplification primers as well as mutation detection (allelic-discrimination) probes need to work together in the same homogeneous condition balancing the need for high amplification efficiency and the capability in distinguishing the

7. As described in Section 5.1 (Primer and probe design guidelines) in Real-Time PCR (Advanced Methods Series) (Dorak MT, Oxford: Taylor & Francis, 2006), real-time PCR has different needs than conventional PCR. Different considerations for real-time PCR include, for example, primer melting temperature, probe melting temperature, amplification product length, and placement of primers and probes.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the captioned patent application or any patent issued therefrom.

8. 9. 2006

Date

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